an amount effective in treating, in a mammal, a staphylococcal infection that is not resistant to said anti-staphylococcal agent and wherein the cell-wall active antibiotic is present in an amount effective in treating, in a mammal, a staphylococcal infection that is not resistant to the cell-wall active antibiotic, and wherein the anti-staphylococcal agent and the cell-wall active antibiotic are co-administered such that said anti-staphylococcal agent and said cell-wall active antibiotic, when co-administered, suppress the formation of staphylococcal strains resistant to said anti-staphylococcal agent, said cell-wall active antibiotic and combinations of said anti-staphylococcal agent and said cell-wall active antibiotic.

25. (New) The method of Claim 24, wherein the anti-staphylococcal agent is one whose activity is mediated by cleavage of the cell wall of staphylococci.

26. (New) The method of Claim 24, wherein the anti-staphylococcal agent is selected from the group consisting of lysostaphin, *lasA* protease and achromopeptidase.

27. (New) The method of Claim 23, wherein said staphylococcal infection comprises a coagulase-negative staphylococcal microorganism, a coagulase-positive staphylococcal microorganism or combinations thereof.

28. (New) The method of Claim 24, wherein said staphylococcal infection comprises a coagulase-negative staphylococcal microorganism, a coagulase-positive staphylococcal microorganism or combinations thereof.--

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REMARKS

Applicants respectfully request that the Examiner consider the foregoing Supplemental Preliminary Amendment upon initial consideration on the merits of the present application. Applicants submit that the Supplemental Preliminary Amendment does not introduce new matter.

Applicants' claimed method treats a staphylococcal infection in a mammal while, at the same time, suppressing the formation of antibiotic-resistant staphylococcal strains. In particular, by co-administering an anti-staphylococcal agent other than a cell-wall active antibiotic together with a cell-wall active antibiotic according to Applicants' invention, the formation of strains of staphylococci resistant to the combination of the anti-staphylococcal agent other than a cell-wall active antibiotic and the cell-wall active antibiotic is suppressed. Furthermore, strains that are resistant to either the anti-staphylococcal agent or the cell-wall active antibiotic are also suppressed.

Accordingly, Applicants submit that this application is in condition for examination and favorable consideration is respectfully requested.

Respectfully submitted,

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MARKED-UP COPY OF PARAGRAPHS, AS AMENDED

Replacement for the second full paragraph at page 3, line 17-page 4, line 5:

--Numerous articles have noted the development of resistance to either lysostaphin or β-lactams, such as methicillin, and the relationship there between. Thus, DeHart, et al., Applied Environmental Microbiology [61, 1475-1479] 61:1475-1479 (1995) noted the development of mutant *S. aureus* recombinant cells that were resistant to lysostaphin, but susceptible to methicillin. Similar phenomenon are reported by Zygmunt, et al., Can. J. Microbio. [13,845-852 (1966)] 13:845-853 (1967), Polak, et al., Diagn. Microbiol. [Infet.] Infect. Dis. 17:265-270 (1993) and [Dickson] Dixon, et al., Yale J. Bio. Med. 41:62-67 (1968). Each of these references, as well as later reports such as Ehlert, J. Bacteriology[,] 179:7573-7576 (1997), note that staphylococci that develop resistance to lysostaphin, either spontaneously or through induced recombination, become susceptible to methicillin treatment, and vice-versa. In all of these references, the uniform suggestion is to follow a course of administration of lysostaphin, even a short one, with administration of methicillin.--

Replacement for the second paragraph at page 10, line 21-page 11, line 10:

--The same unpredicted result has been demonstrated through *in vivo* experiments based on the widely accepted rabbit model of aortic valve [endoearditis] endocarditis, predictive of *in vivo* administration to humans. When administered to staphylococcal infected rabbits at low doses (1 mg/kg bid, as compared with a minimum value of 5 mg/kg tid for sterilization), lysostaphin, as representative of anti-staphylococcal agents acting by cleavage of the glycine-containing cross-links, resulted in recovery of a number of resistant

colonies, with high counts in vegetations and kidneys, while the same dosage together with nafcillin (a β-lactam) gave sterile kidneys, some sterile vegetations, and no resistant strains recovered. The simultaneous treatment of staphylococcal infection with suppression of resistant strain formation is an exciting and widely useful invention nowhere predicted in the art. This invention offers the possibility of treating staphylococcal infections while suppressing the generation of strains resistant to any or all active agents administered.--

MARKED-UP COPY OF AMENDED CLAIMS

3. (Amended) The method of Claim [1] 23, wherein said administration is achieved through any one or more of intravenous (IV), intramuscular (IM), subcutaneous (SC), intraperitoneal (IP), intrathecal or topical administration.

6. (Amended) The method of Claim [1] 23, wherein said cell-wall active antibiotic is a β-lactam or a glycopeptide.

10. (Amended) The method of Claim [1] 23, wherein said staphylococcal infection is mediated by at least one *S. aureus* microorganism.

11. (Amended) The method of Claim [1] 23, wherein said staphylococcal infection is mediated by at least one coagulase-negative staphylococcal microorganism.